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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,950	01/25/2002	Bryan Greener	P07504US00/BAS	8762

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EXAMINER

ZUCKER, PAUL A

ART UNIT

PAPER NUMBER

1621

DATE MAILED: 06/20/2003

4

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Applicati n N .

10/031,950

Applicant(s)

GREENER, BRYAN

Examin r

Paul A. Zucker

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-15 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-15 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All   b) ☐ Some \*   c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

## **DETAILED ACTION**

### ***Information Disclosure Statement***

1. The references cited in the International Search Report have been considered, but will not be listed on any patent resulting from this application because they were not provided on a separate list in compliance with 37 CFR 1.98(a)(1). In order to have the references printed on such resulting patent, a separate listing, preferably on a PTO-1449 form, must be filed within the set period for reply to this Office action.

### ***Specification***

2. Applicant should amend the specification to reflect the status of the application by inserting the phrase "This application is a 371 of PCT/GB00/02881 filed 07/26/2000" as the first line of specification.
3. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.
4. The disclosure is objected to because of the following informalities: The specification lacks a section entitled "Brief Description of the Drawings" describing the drawings. Appropriate correction is required.

### ***Claim Objections***

5. Claim 5 is objected to because of the following informalities: The word "lease" in line 10 is misspelled. Appropriate correction is required.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 1-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1 and 5 recite the limitation "supramolecular assembly" in lines 1 and 2, respectively. The term "supramolecular assembly" is undefined. Claims 1 and 5 and their dependents are therefore rendered indefinite.
7. Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 4 recites the limitation "hydrophobic moiety" in line 1. There is insufficient antecedent basis for this limitation in the claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1- 3 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the compounds exemplified in the specification, does not reasonably provide enablement for all possible compounds having the ability to form supramolecular assemblies. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Applicants provide sufficient guidance (Specification, page 9, line 17-page

13, line 14) on how to make the oligomers derived from 2,5-dihydroxybenzoic acid and dodecanoyl chloride. No guidance, however, is provided for any other compound. No guidance is provided for determining which other compounds meet the limitations of the instant claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue."

These factors include, but are not limited to:

- a. **The breadth of the claims:** In the instant case the claims are extremely broad. All classes of compounds are encompassed including water, proteins, DNA, complex organic compounds and inorganic compounds.
- b. **The nature of the invention:** In the instant compounds are claimed which are capable of forming supramolecular assemblies. The only criteria is that these compounds contain regularly spaced multiple hydrogen bonding sites. All classes of compounds are encompassed including proteins, DNA, complex organic compounds and inorganic compounds such as water.
- c. **The level of predictability in the art:** With regard to predictability, the ability to predict whether a compound will form supramolecular structures depends not only on the knowledge of hydrogen bonding sites but the energetics of various conformational states and therefore can be seen as unpredictable over the variety of structures encompassed by the instant claims

- d. **The amount of direction provided by the inventor:** The inventors provide a sufficient description (Specification, page 9, line 17-page 13, line 14) of how to make the oligomers derived from 2,5-dihydroxybenzoic acid and dodecanoyl chloride. No guidance is provided for any other compound. No guidance is provided for determining which other compounds meet the limitations of the instant claims
- e. **The existence of working examples:** Applicants provide several working examples demonstrating how to make the oligomers derived from 2,5-dihydroxybenzoic acid and dodecanoyl chloride. No other working examples demonstrating how to make other compounds, such as proteins, are provided.
- f. **The quantity of experimentation needed to make or use the invention based on the content of the disclosure:** Because of the large number of compounds claimed and the lack of guidance in determining which meet the limitations of the claims, one of ordinary skill in the art would have to engage in undue experimentation in order to determine which compounds meet the claim limitation. Further undue experimentation is required to make those compounds.

Based on the above analysis, the Examiner concludes that undue experimentation is required to make and use the invention commensurate in scope with the instant claims.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Hawley (The Condensed Chemical Dictionary, 8<sup>th</sup> edition, Van Nostrand Reinhold Company, New York, 1971, page 455). Hawley discloses (Page 455, Column 1, lines 2-19) that water forms a hydrogen bonded network. Water has multiple hydrogen bonding sites 2 donor sites (hydrogen atoms) and one acceptor site (oxygen atom, a non-terminal site). Liquid water therefore forms a supramolecular assembly. Ice demonstrates even higher levels of organization. Water is generally recognized in the art as pharmacologically acceptable. Claims 1 and 2 are therefore anticipated by Hawley.
10. Claims 1-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Solomons (Organic Chemistry, 5<sup>th</sup> edition, John Wiley & Sons, Inc., New York, 1992, pages 1092-1133). Solomons discloses (Page 1129, Fig 24.15, lower left corner, and caption) the mechanism of action of lysozyme. Solomons discloses the hydrogen bonding between lysozyme and its substrate. Lysozyme is composed of amino acids which contain hydrogen bonding sites separated by hydrophobic moieties (the  $\alpha$  carbons). Glutamic acid (See Figure 1(b)) can be considered a functional derivative of an alkyl diacid. Claims 1-6 are therefore anticipated by Solomons.

11. Claims 1,3-8,10 and 13 are rejected as being anticipated by Gennari et al (Journal of Organic Chemistry, Acceleration of Hemiacetal Cleavage through Hydrogen Bonding: A New Synthetic Catalyst with Balanced Conformational Flexibility and Preorganization, 1991, 56, pages 3201-3203). Gennari discloses (Page 3201, bottom right, Scheme I, center) the polyether polybenzoate compound 6. This compound has repeating aromatic units of instant formula (II) which are linked with hydrophobic linkers. Gennari further discloses (Page 3202, paragraph bridging right and left columns) that polymers of this material are formed in the macrocyclization reaction. Because the structural requirements are met by the compounds disclosed by Genarri, the Examiner presumes that they have the required properties. Claims 1,3-8,10 and 13 are therefore anticipated by Gennari.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

12. Claims 1-3, 5-10 and 13-15 are rejected under 35 U.S.C. 102(e) as being anticipated by Hutchins et al (US 6,124,137 09-2000). Hutchins discloses (Fig. 23 and column 33, lines 23-36) the compound MAP-dihydroxybenzoic acid. This compound has 2,5 dihydroxybenzoic acid-derived termini (corresponding to instant variable group A) containing hydroxy groups, which are linked by amino acids which have regularly spaced hydrogen bonding groups (>3), spaced by hydrophobic moieties (the  $\alpha$  carbons). Amino acids are generally considered pharmacologically acceptable. The aggregation of molecules of this compound to form supramolecular assemblies is



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presumed to be an inherent property since the molecule possesses the instantly required functionality. Hutchins further discloses (Column 33, lines 23-36) the manufacture of probe tips (artifacts) using this compound. Claims 1-3, 5-10 and 13-15 are therefore anticipated by Hutchins.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35

U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

13. Claims 1-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Graham (US 4,150,108 04-1979).

Instantly claimed are compounds of general formula  $A-X-(N-X)_n-A$  which are capable of forming supramolecular structures, where N, A, n and X are as defined in the claims.

Graham teaches (Column 1, lines 27-43) medicinal compositions comprising steroids trapped in a polymer matrix. Graham further teaches that this polymer matrix can be formed from dihydropyran and mixtures of compounds including 2,3-dihydroxybenzoic acid, 2,5-dihydroxybenzoic acid and adipic acid (hexanedioic acid) among others. Employing either 2,3-dihydroxybenzoic acid or 2,5-dihydroxybenzoic acid with adipic acid produces polymers that meet the limitations of the instant claims. Presumably they would be capable of forming supramolecular structures since they possess multiple hydrogen bonding sites. Because of the broad way in which the variable groups A and N are defined (they possess hydrogen bonding sites) the substructure derived from dihydropyran is considered to be encompassed by the instant claims. The medicinal composition itself constitutes the claimed aggregation of compounds as well as the claimed artifact (something of unnatural origin which result from extraneous (human) agency).

One of ordinary skill in the art would have been motivated to make the instant compounds by Graham's teaching that they have value in timed release pharmaceutical compositions. There would have been reasonable expectation for success because Graham specifically suggests the suitability of the instant compounds for the purpose. The instantly claimed compounds would therefore have been obvious to one of ordinary skill in the art.

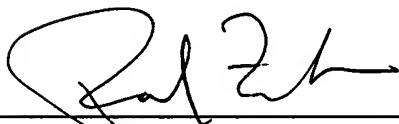
### ***Conclusion***

14. Claims 1-15 are pending. Claims 1-15 are rejected. Claim 5 is objected to.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul A. Zucker whose telephone number is 703-306-0512. The examiner can normally be reached on Monday-Friday 7:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann R. Richter can be reached on 703-308-4532. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.



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Paul A. Zucker, Ph.D.  
Patent Examiner  
Technology Center 1600

June 17, 2003